CORRECTED VERSION*

PCT

WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 :
C07D 401/04, 417/04, 403/04, 279/16, 277/62, 239/72, 235/04, 249/16, 327/06, A61K 31/38, 31/41, 31/415, 31/42, 31/425, 31/47, 31/505, 31/40, 31/535, 31/54

A1

(11) International Publication Number: WO 97/48694

(43) International Publication Date: 24 December 1997 (24.12.97)

(21) International Application Number: PCT/US97/10643

(22) International Filing Date: 20 June 1997 (20.06.97)

(30) Priority Data:
60/016,088 20 June 1996 (20.06.96) US

(60) Parent Application or Grant
(63) Related by Continuation
US 60/016,088 (CIP)
Filed on 20 June 1996 (20.06.96)

(71) Applicant *(for all designated States except US)*: BOARD OF REGENTS, THE UNIVERSITY OF TEXAS SYSTEM [US/US]; 201 West 7th Street, Austin, TX 78701 (US).

(72) Inventors; and
(75) Inventors/Applicants *(for US only)*: KERWIN, Sean [US/US]; 703 Ivy Court, Round Rock, TX 78681 (US). HURLEY, Laurence, H. [US/US]; 5915 N.W. Place, Austin, TX 78731 (US). DeLUCA, Mark, R. [US/US]; 3806 Oak Meadow Drive, Round Rock, TX 78681 (US). MOORE, Bob, M., III [US/US]; 9815 Copper Creek Drive, Austin, TX 78729 (US). MUNDY, Gregory [US/US]; 3719 Morgans Creek, San Antonio, TX 78230 (US).

(74) Agent: MAYFIELD, Denise; Akin, Gump, Strauss, Hauer & Feld, L.L.P., 1900 Frost Bank Plaza, 816 Congress Avenue, Austin, TX 78701 (US).

(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, ARIPO patent (GH, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).

Published
With international search report.
Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(54) Title: COMPOUNDS AND METHODS FOR PROVIDING PHARMACOLOGICALLY ACTIVE PREPARATIONS AND USES THEREOF

(57) Abstract

The present invention relates to pharmacologically active compounds which are capable of binding to nuclear hormone receptors and are useful for the stimulation of osteoblast proliferation and ultimately bone growth. This invention also relates to the use of such compounds for the treatment or prevention of diseases and/or disorders associated with nuclear hormone receptor families.

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	**ES**	Spain	**LS**	Lesotho	**SI**	Slovenia
AM	Armenia	**FI**	Finland	**LT**	Lithuania	**SK**	Slovakia
AT	Austria	**FR**	France	**LU**	Luxembourg	**SN**	Senegal
AU	Australia	**GA**	Gabon	**LV**	Latvia	**SZ**	Swaziland
AZ	Azerbaijan	**GB**	United Kingdom	**MC**	Monaco	**TD**	Chad
BA	Bosnia and Herzegovina	**GE**	Georgia	**MD**	Republic of Moldova	**TG**	Togo
BB	Barbados	**GH**	Ghana	**MG**	Madagascar	**TJ**	Tajikistan
BE	Belgium	**GN**	Guinea	**MK**	The former Yugoslav Republic of Macedonia	**TM**	Turkmenistan
BF	Burkina Faso	**GR**	Greece			**TR**	Turkey
BG	Bulgaria	**HU**	Hungary	**ML**	Mali	**TT**	Trinidad and Tobago
BJ	Benin	**IE**	Ireland	**MN**	Mongolia	**UA**	Ukraine
BR	Brazil	**IL**	Israel	**MR**	Mauritania	**UG**	Uganda
BY	Belarus	**IS**	Iceland	**MW**	Malawi	**US**	United States of America
CA	Canada	**IT**	Italy	**MX**	Mexico	**UZ**	Uzbekistan
CF	Central African Republic	**JP**	Japan	**NE**	Niger	**VN**	Viet Nam
CG	Congo	**KE**	Kenya	**NL**	Netherlands	**YU**	Yugoslavia
CH	Switzerland	**KG**	Kyrgyzstan	**NO**	Norway	**ZW**	Zimbabwe
CI	Côte d'Ivoire	**KP**	Democratic People's Republic of Korea	**NZ**	New Zealand		
CM	Cameroon			**PL**	Poland		
CN	China	**KR**	Republic of Korea	**PT**	Portugal		
CU	Cuba	**KZ**	Kazakstan	**RO**	Romania		
CZ	Czech Republic	**LC**	Saint Lucia	**RU**	Russian Federation		
DE	Germany	**LI**	Liechtenstein	**SD**	Sudan		
DK	Denmark	**LK**	Sri Lanka	**SE**	Sweden		
EE	Estonia	**LR**	Liberia	**SG**	Singapore		

The Delphion Integrated View

Title: **WO9748694A1: COMPOUNDS AND METHODS FOR PROVIDING PHARMACOLOGICALLY ACTIVE PREPARATIONS AND USES THEREOF**[French]

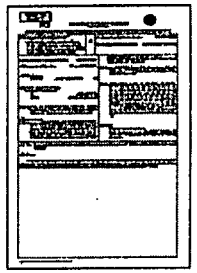
Derwent Title: Stimulation of osteoblast proliferation and BMP-2 promoter activity - by administration of aryl derivatives [Derwent Record]

Country: **WO** World Intellectual Property Organization (WIPO)

Kind: **A1** Publ.of the Int.Appl. with Int.search report

Inventor: **KERWIN, Sean**; 703 Ivy Court, Round Rock, TX 78681, United States of America
HURLEY, Laurence, H.; 5915 N.W. Place, Austin, TX 78731, United States of America
DeLUCA, Mark, R.; 3806 Oak Meadow Drive, Round Rock, TX 78681, United States of America
MOORE, Bob, M., III; 9815 Copper Creek Drive, Austin, TX 78729, United States of America

Assignee: **BOARD OF REGENTS, THE UNIVERSITY OF TEXAS SYSTEM**, 201 West 7th Street, Austin, TX 78701, United States of America
News, Profiles, Stocks and More about this company



High Resolution

Low Resolution

120 pages

Published / Filed: **1997-12-24** / 1997-06-20

Application Number: **WO1997US0010643**

IPC Code: **C07D 401/04;** C07D 417/04; C07D 403/04; C07D 279/16; C07D 277/62; C07D 239/72; C07D 235/04; C07D 249/16; C07D 327/06; A61K 31/38; A61K 31/41; A61K 31/415; A61K 31/42; A61K 31/425; A61K 31/47; A61K 31/505; A61K 31/40; A61K 31/535; A61K 31/54;

ECLA Code: **A61K31/428**; A61K31/47+A; C07D215/38C; C07D277/82;

Priority Number: 1996-06- **US1996000016088P**

Abstract: The present invention relates to pharmacologically active compounds which are capable of binding to nuclear hormone

receptors and are useful for the stimulation of osteoblast proliferation and ultimately bone growth. This invention also relates to the use of such compounds for the treatment or prevention of diseases and/or disorders associated with nuclear hormone receptor families. [French]

Attorney, Agent or Firm: **MAYFIELD, Denise** ;

INPADOC Legal Status: Show legal status actions **Get Now:** Family Legal Status Report

Designated Country: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN, **European patent:** AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE, **OAPI patent:** BF BJ CF CG CI CM GA GN ML MR NE SN TD TG, **ARIPO patent:** GH KE LS MW SD SZ UG ZW, **Eurasian patent:** AM AZ BY KG KZ MD RU TJ TM

Family: Show 17 known family members

Description Expand description

+ TITLE COMPOUNDS AND METHODS FOR PROVIDING PHARMACOLOGICALLY ACTIVE PREPARATIONS AND USES THEREOF

+ FIELD OF THE INVENTION

The present invention relates to compounds and their use for the treatment of nuclear hormone receptor (NHR) family associated disorders. More specifically, the present invention relates to compounds having a particular 3-dimensional spatial orientation that are capable of binding to and thus altering the function of NHRs. Such compounds would be useful as therapeutic agents for disorders associated with NHRs such as the retinoid x receptor (RXR). The invention also relates to compositions and methods for the treatment or prophylaxis of osteoporosis, bone loss, arthritis, inflammation, cancer and skin conditions.

+ BACKGROUND OF THE INVENTION

+ DESCRIPTION OF THE PRIOR ART

+ SUMMARY OF THE INVENTION

+ BRIEF DESCRIPTION OF THE DRAWINGS

+ DETAILED DESCRIPTION OF THE INVENTION

First Claim: Show all claims 1.A method for stimulating osteoblast proliferation comprising: selecting substances of the general formula I X-L-Z, Formula I wherein: lo X is selected from the group consisting of: RI R5 R2 R3 R4 RI RI 0 RI 5 R3 S R5 R2 R2 0@@k Z R2 @Pe N @'% R2 R-i R3 t R3 RI R3 R4 R5 R3 R4 R3 R4 R2 N N @t o r R2 R2 N R2 R3 N I 6H k5 L is selected from the group consisting of: N NV 1 AS`O@ 0OA7 AN or a single bond I k6 1 5 94

Z is selected from the group consisting of: R8 R8 R13 R8 R9 R13 N R9 N R9 or R12 RIO RIO RIO 11 12 RI 12 RI I wherein: R1 is selected from the group consisting of: HI OHf Cl-C4 alkyl, Cl-C4 alkoxy, Cl-C4 alkylthio, halo and (Cl-Cl2)alkyl-carbonyloxy; R' is selected from the group consisting of: HI OH, halo, Cl-C6 alkyl, Cl-C6 alkenyl, Cl-C6 alkoxy and (Cl-Cl2)alkyl-carbonyloxy; R' is selected from the group consisting of: H, OH, halo, Cl-C6 alkyl, Cl-C6 alkoxy, Cl-C6 alkenyl and (Cl-Cl2)alkyl-carbonyloxy; R' is selected from the group consisting of: HI OH, halo, Cl-C6 alkyl, Cl-C6 alkoxy and (Cl-Cl2)alkylcarbonyloxy; R5 is selected from the group consisting of: H. halo, Cl-C6 alkyl, Cl-C6 alkoxy, -OC(=O)Me, phthalimide and (Cl-Cl2)alkyl-carbonyloxy; R6 is selected from the group consisting of: HI OH, -NH21 Cl-C4 alkyl and Cl-C4 alkoxy; R7 is selected from the group consisting of: HI Cl-C4 alkyl, (Cl-C4)alkyl-carbonyl and (C7ClO)arylalkyl; R8 is selected from the group consisting of: H, OH, halo, -CF3t Cl-C4 haloalkyl, Cl-C4 alkyl, Cl-C4 alkoxy, -NHC(=O)Me and -N(Cl-C4 alkyl)2; R' is selected from the group consisting of: HI OH, halo, -CN, -NO2i Cl-C4 haloalkyl, Cl-C8 alkyl, Cl-C8 alkoxy, -NHC(=O)Me and -OC(=O)Me; 3o R'0 is selected from the group consisting of: HI OH, halo, -CNf -NO2 I Cl-C4 haloalkyl, -CO2Hj Cl-C12 alkyl, Cl-C12 alkoxy, phenyl, Cl-C12 alkenyl, (Cl95 C4)alkoxycarbonyl, -NHC(=O)Me, (Cl-Malkylcarbonyl, (ClC12)alkylcarbonyloxy and heteroaryl; R" is selected from the group consisting of: Hi OH, halo, Cl-C4 haloalkyl, -CF3, Cl-C4 alkyl, -NH2, Cl-C4 alkoxy, -NHC(=O)Me, Cl-C4 alkenyl, (Cl-Malkoxycarbonyl, (Cl-C4)alkylcarbonyl, and (Cl-C4) alkylcarbonyloxy; R12 is selected from the group consisting of: Hi OHf -NH2 i Cl-C4 alkyl, Cl-C4 alkoxy, and (ClC4)alkylcarbonyl; and R13 is selected from the group consisting of: Hi OH, halo, -NH2, Cl-C4 alkyl, Cl-C4 alkoxy, -N(Cl-C4 alkyl)2; and exposing cells comprising osteoblast cells to an effective amount of the pharmacologically active compound. 1 5 †

Forward References:

Go to Result Set: Forward references (13)

PDF	Patent	Pub.Date	Inventor	Assignee	Title
	US6780883	2004-08-24	Booth; Richard John	Warner-Lambert Company	Amide inhibitors of microsomal triglyceride transfer protein
	US6774237	2004-08-10	Renhowe; Paul A.	Chiron Corporation	Quinolinone derivatives
	US6762194	2004-07-13	Renhowe; Paul A.	Chiron Corporation	Quinolinone derivatives
			Renhowe; Paul		

	US6759417	2004-07-06	A.	Chiron Corporation	Heterocyclic compounds
	US6756383	2004-06-29	Renhowe; Paul A.	Chiron Corporation	Heterocyclic derivatives of quinolinone benimidazoles
	US6670398	2003-12-30	Edwards; David B.	AtheroGenics, Inc.	Compounds and methods for treating transplant rejection
	US6656904	2003-12-02	Mundy; Gregory R.	OsteoScreen, Inc.	Inhibitors of proteasomal activity for stimulating bone and hair growth
	US6617352	2003-09-09	Somers; Patricia K.	Atherogenics, Inc.	Compounds and methods for the inhibition of the expression of VCAM-1
	US6605617	2003-08-12	Renhowe; Paul A.	Chiron Corporation	Quinolinone derivatives
	US6602914	2003-08-05	Meng; Charles Q.	AtheroGenics, Inc.	Compounds and methods for the inhibition of the expression of VCAM-1
	US6548699	2003-04-15	Somers; Patricia K.	Atherogenics, Inc.	Compounds and methods for the inhibition of the expression of VCAM-1
	US6462019	2002-10-08	Mundy; Gregory R.	OsteoScreen, Inc.	Inhibitors of proteasomal activity and production for stimulating bone growth
	US6376476	2002-04-23	Gasper; Shirley R.	ZymoGenetics Corporation	Isoprenoid pathway inhibitors for stimulating bone growth

Other Abstract Info: CHEMABS 128(07)075390X CHEMABS 128(07)075390X DERABS C1998-086619 DERABS C1998-